

In the Specification:

Please replace the paragraphs at page 5, lines 2-20 with the following paragraphs:

According to a first aspect of the present invention there is provided a histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7} M and which has a binding site comprising amino acid residues phenylalanine, isoleucine or leucine at position I, tryptophan at position II and aspartate or glutamate at positions III and IV wherein residues I to IV are positioned substantially the same as residues 108, 42, 39 and 82 respectively in either of SEQ. ID. Nos 1 or 2, or residues 107, 41, 38 and 78 in SEQ ID 3 or residues ~~122, 54, 50 and 95~~ 139, 71, 67, and 112 in SEQ ID NO: 4, and functional equivalents thereof. Hereafter, this binding site will be referred to as the “first binding site”. The proteins identified in SEQ IDs 1 to 4 are known as FS-HBP1, FS-HBP2, MS-HBP and D.RET6 respectively.

According to a second aspect of the present invention there is provided a histamine or serotonin binding compound capable of binding to histamine or serotonin with a dissociation constant of less than 10^{-7} M and which has a binding site comprising amino acid residues phenylalanine or isoleucine at residue I, tryptophan at residue II and aspartate or glutamate at residues III and IV wherein residues I to IV are positioned substantially the same as residues 98, 137, 24 and 120 respectively in either of SEQ. ID. Nos 1 or 2, or residues 95, 138, 23 and 120 in SEQ. ID. 3 or residues 129, 166, 52, and 152 ~~112, 149, 35 and 135~~ in SEQ ID NO: SEQ-ID. 4, and functional equivalents thereof. Hereafter, this binding site will be referred to as the “second binding site”.

Please replace the paragraph at page 7, lines 24-32 with the following paragraph:

Accordingly, it is contemplated that any molecular framework capable of retaining these amino acid side-chains in the necessary positions for binding to histamine or serotonin will be suitable for use in accordance with the present invention. Of particular suitability will be cyclic peptides held in a precise framework by their linking groups and bonds. The amino acid side chains may be held in a position substantially identical to their

position in the histamine or serotonin binding site of native histamine or serotonin binding compounds. Preferably, the cyclic peptides comprise between 6 and 30 amino acids, preferably between 8 and 20 amino acids. Of particular suitability is the cyclic octapeptide Ala-Glu-Ala-Phe-Ala-Glu-Ala-Trp (SEQ ID NO: 31).

Please replace page 19, line 12 through to page 20, line 2 with the following:

Figure 1 is the nucleic and amino acid sequence of FS-HBP1 (~~SEQ. ID. 1~~) (SEQ ID NO: 12 and SEQ ID NO: 1, respectively), showing sequencing primers and sequencing strategy.

Figure 2 is the nucleic and amino acid sequence of FS-HBP2 (~~SEQ ID 2~~) (SEQ ID NO: 13 and SEQ ID NO: 2, respectively), showing sequencing primers and sequencing strategy.

Figure 3 is the nucleic and amino acid sequence of MS-HBP1 (~~SEQ ID 3~~) (SEQ ID NO: 14 and SEQ ID NO: 3, respectively), showing sequencing primers and sequencing strategy.

Figure 4 is the nucleic and amino acid sequence of D.RET6 (~~SEQ ID 4~~) (SEQ ID NO: 15 and SEQ ID NO: 4, respectively), showing sequencing primers and sequencing strategy.

Figure 5 is the nucleic and amino acid sequence of ra-RES (~~SEQ. ID. 5~~) (SEQ ID NO: 16 and SEQ ID NO: 5, respectively). Asparagines that are part of putative glycosylation recognition sites are underlined and shown in italics. The squiggly line denotes a possible amidation site I; the double line indicates the putative polyadenylation signal and the polyA-tail is shown in bold letter type.

Figure 6 is the nucleic and amino acid sequence of Av-HBP (~~SEQ. ID. 6~~) (SEQ ID NO: 17 and SEQ ID NO: 6, respectively). Sequence of the Av-HBP cDNA and its inferred primary structure. The cDNA has a remarkably long non-coding region, downstream of the stop codon.

Figure 7 is the nucleic and amino acid sequence of Ih/Bm-HBP1 (~~SEQ. ID. 7~~) (SEQ ID NO: 18 and SEQ ID NO: 7, respectively).

Figure 8 is the nucleic and amino acid sequence of Ih/Bm-HBP2 (~~SEQ. ID. 8~~) (SEQ ID NO: 19 and SEQ ID NO: 8, respectively).

Figure 9 is the nucleic and amino acid sequence of Ih/Bm-HBP3 (~~SEQ. ID. 9~~) (SEQ ID NO: 20 and SEQ ID NO: 9, respectively).

Figure 10 is the nucleic and amino acid sequence of Ih/Bm-HBP4 (~~SEQ. ID. 10~~) (SEQ ID NO: 21 and SEQ ID NO: 10, respectively).

Figure 11 is the nucleic and amino acid sequence of Ih/Bm-HBP5 (~~SEQ. ID. 11~~) (SEQ ID NO: 22 and SEQ ID NO: 11, respectively).

Please replace page 21, lines 16-19 with the following:

Figure 22: An alignment of the cDNA-inferred amino acid sequences of the various HBPs, created using the pileup commands of the Genetics Computer Group. (1994). Program Manual for the Wisconsin Package, version 8. (575 Science Drive, Madison, Wisconsin, USA 53711). The amino acid sequences of ihhbp3, ihhbp4, ihhbp5, FS-HBP1, FS-HBP2, MS-HBP1, ihhbp1, ihhbp2, D-RET6, avhbp, and ra-res correspond to SEQ ID NOs: 9, 10, 11, 1, 2, 3, 7, 8, 4, 6, and 5, respectively.

Please replace the paragraph at page 22, lines 7-14 with the following paragraph:

Using the RNase Total Pure extraction kit (Bioline Ltd., UK), total RNA was isolated from salivary glands of partially fed *Amblyomma variegatum*, *Ixodes hexagonus* and *Boophilus microplus* ticks. The RNA samples were submitted to reverse-transcriptase polymerase chain reactions (RT-PCR), using the Titan One-Tube RT-PCR system (Boehringer Mannheim) and degenerate primers:

5'-AA YGGNGARCA YCARGAYGCNTGGAA (SEQ ID NO: 23); and

5'-KTRTMRTCNGTNR YCCANARYTCRTA (SEQ ID NO: 24), the design of which was based on conserved domains in the *Rhipicephalus appendiculatus* HBPs.

Please replace the paragraph at page 23, lines 1-7 with the following paragraph:

Using an *E. coli*-based expression system, the DNA sequence encoding D.RET6 (from Glu29 to Leu109) was subcloned as a *Bcl*II/ *Xho*I fragment into *Bam*HI/ *Xho*I -digested pET-23 a (+) in the same reading frame as the 6x His tag using the PCR technique with the following primers, 5'-TATATGATCAGAAAACCCGCTCTGGG-3' (SEQ ID NO: 25) and 5'TATA CTGAGCCA GGGTTCGCCGT-3' (SEQ ID NO: 26) (the enzyme recognition sites are underlined.). The recombinant plasmid was transformed into host strain AD494(DE3) pLysS, which uses the T7 system, and success of the procedure was confirmed by sequencing.

Please replace the paragraph at page 23, lines 16-19 with the following paragraph:

D.RET6 was also expressed in the baculovirus expression system. The DNA fragment containing the complete coding sequence of D.RET6 was amplified using the oligonucleotides: 5'-TATGAAGATGCAGGTAGTGC-3' (SEQ ID NO: 27) and: 5'-ATATGATCAGCCAGGGTTCGCCGT-3' (SEQ ID NO: 28).

Please replace the paragraph at page 25, lines 17-25 with the following paragraph:

The coding region of the Av-HBP cDNA was PCR amplified (95 °C for 30", 50 °C for 30", 72 °C for 30"; 18 cycles) using a forward primer designed to add a *Sac* I site upstream of the start codon (5'- TATGAGCTCATGAACTCTGCCTTGTGG (SEQ ID NO: 29); the *Sac*I site is underlined), and a reverse primer (5'- TATGGATCCGGGGTGGCCTCACCG) (SEQ ID NO: 30) containing a *Bam*HI site (underlined). The product was ligated in between the *Sac* I and *Bam*HI sites of the pAcCl29.1 transfer vector (Livingstone and Jones, 1989) which had been modified by the insertion of six histidine codons and a stop codon, downstream of the *Bam*HI recognition site (see original patent). This resulted in the addition of the sequence Ile-(His)₆ to the carboxy- terminus of Av-HBP.